The opinion in support of the decision being entered today is *not* binding precedent of the Board.

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte BEN- ZION DOLITZKY, JUDITH ARONHIME, SHLOMIT WIZEL, and GENNADY NISNEVISH

Appeal 2007-1817
Application 10/045,510
Technology Center 1600

Decided: September 5, 2007

Before DEMETRA J. MILLS, NANCY J. LINCK, and RICHARD M. LEBOVITZ, *Administrative Patent Judges*.

MILLS, *Administrative Patent Judge*.

DECISION ON APPEAL

This appeal under 35 U.S.C. § 134 involves claims 1-2 and 95-98 the only claims pending in this application. We have jurisdiction under 35 U.S.C. § 6(b).

Representative claims 1 and 95 read as follows:

1. A crystalline venlaflaxine base wherein the venlaflaxine base is in the form of white crystals.

95. White crystalline solid venlafaxine base prepared by a method comprising the steps of:
a) providing a solution of venlafaxine hydrochloride in water,
b) combining the solution of venlafaxine hydrochloride with sodium hydroxide,
c) extracting the combination with an organic solvent to obtain extract,
d) drying the extract,
e) evaporating the extract to obtain a residue,
f) combining the residue with an alkane, and
g) crystallizing venlafaxine base that is a white crystalline solid from the combination of residue and alkane.

Cited References:

Jerussi	WO 00/32555	Jun. 8, 2000

Grounds of Rejection

Claims 1-2 and 95-98 are rejected under 35 U.S.C. § 103(a) as obvious over Jerussi.

We affirm.

DISCUSSION

Venlafaxine is a commercial product sold prior to Appellants' filing date by Wyeth under the tradename Effexor®. Venlafaxine acts by inhibiting re-uptake of norepinephrine and serotonin, and is an alternative to

tricyclic antidepressants and selective re-uptake inhibitors. (Specification 1.[1])

Appellants state that they have "found that crystalline venlafaxine can be prepared from venlafaxine hydrochloride by methylation of N,N-didesmethyl venlafaxine by means of a novel process." (Specification 2.) One aspect of the invention relates to "essentially pure venlafaxine." (Specification 2.)

Obviousness

Claims 1 and 2

Claim 1 is to "crystalline venlafaxine base . . . in the form of white crystals." Claim 2 additionally requires a "purity of greater than about 99.3%." In the Specification, Appellants do not describe how "color" is determined and do not define "crystalline." Further, they do not limit their claims to a polymorph or to any specific isomer.

According to the Examiner, the "prior art generally teaches that venlafaxine is a well-known compound for the treatment of depression." (Answer 3.) The Examiner found Jerussi discloses venlafaxine as a "pale yellow solid." (*Id.* (citing Jerussi, at 23).) The Examiner posited that the "purity appears to be less than what is presently claimed and the color is not white." (*Id.*) The Examiner found the difference in purity is that of 99.3%, as in Appellants' claim 2, versus an unknown purity of the venlafaxine compound of Jerussi. (Answer 3.)

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[1] Venlafaxine is incorrectly named in the Specification, as it contains a 4-methoxyphenyl group, not a "4-ethyoxyphenyl" group. (Specification 1; *see also* Br. 2 (repeating the same error).)

The Examiner further found that one of ordinary skill in the art would correlate the compound color with the purity of the compound and that an "ordinary skilled artisan generally would expect pure compounds to be white." (*Id.*) The Examiner argued the corollary that compounds with impurities have color. (Answer 3.) The Examiner concludes "it would have been obvious to one having ordinary skill in the art at the time [the] application was made to have used well-known techniques of purification, in order to make a very pure compound of venlafaxine to eliminate the possibility of side effects that might be associated with the impurities."[2] (*Id.* at 3-4.)

Appellants contend that the Examiner erroneously equates color and general purity and argues that crystallinity alone may dictate a compound's color. (Br. 8-10.) Appellants argue they do not claim "venlafaxine of a different purity." (Br. 10.) Rather, they argue their claimed compound differs "in both color and crystallinity." (Br. 4.)

In appropriate circumstances, a single prior art reference can render a claim obvious. *See, e.g., B.F. Goodrich Co. v. Aircraft Braking Sys.* Corp., 72 F.3d 1577, 1582, 37 USPQ2d 1314, 1318 (Fed. Cir. 1996); *In re O'Farrell*, 853 F.2d 894, 902, 7 USPQ2d 1673, 1680 (Fed. Cir. 1988). However, there must be a showing of a suggestion or motivation to modify

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[2] *Hawley's Condensed Chemical Dictionary,* 12th ed., Van Nostrand Reinhold Company, New York, New York, p. 977 (1993), defines "purification" as "[r]emoval of extraneous materials (impurities) from a substance or mixture...Though absolute purity is impossible to attain, a number of standard procedures exist for approaching it to the extent of 1 ppm of impurity or less. The following fractionation techniques are used: crystallization, precipitation, distillation, adsorption (various types of chromatography), extraction, electrophoresis and thermal diffusion.

the teachings of that reference to the claimed invention in order to support the obviousness conclusion. *See B.F. Goodrich*, 72 F.3d at 1582, 37 USPQ2d at 1318. This suggestion or motivation may be derived from the prior art reference itself, *O'Farrell*, 853 F.3d at 902, 7 USPQ2d at 1680, from the knowledge of one of ordinary skill in the art, or from the nature of the problem to be solved. *Pro-Mold & Tool Co. v. Great Lakes Plastics, Inc.*, 75 F.3d 1568, 1573, 37 USPQ2d 1626, 1630 (Fed. Cir. 1996). Determining whether there is a suggestion or motivation to modify a prior art reference is one aspect of determining the scope and content of the prior art, a fact question subsidiary to the ultimate conclusion of obviousness. With this as background, we analyze the prior art applied by the examiner in the rejection of the claims on appeal.

The Cited Prior Art: Jerussi

Jerussi is representative of the scope and content of the prior art.[3] Jerussi focuses on the preparation of "optically pure derivatives of (+)-venlafaxine with high purity and in high yield." (Jerussi, at 3.) Thus, Jerussi does not further purify racemic venlafaxine (*id.* at 23), but rather *obtains (+)-venlafaxine as a "colorless solid" with 99.95% purity,* using Appellants' preferred extraction solvent, ethyl acetate (*id.* at 24). Jerussi then uses (+)-venlafaxine to prepare derivatives of venlafaxine. In one example, describing the preparation of 1-[cyano-4(4-methoxyphenyl)

[3] Appellants identify another reference that discloses venlafaxine, U.S. 4,525,186 (Specification 1). Example 33 (col. 20) discloses the resolution of racemic venlafaxine. Appellants do not distinguish this teaching but merely state "the '186 patent does not describe whether the venlafaxine so obtained is solid" (Spec. 1). Additionally, we note Wyeth's commercial product is prior art to this application.

methyl]cyclohexanol (a starting material for the preparation of venlafaxine), Jerussi extracts the product with ethyl acetate and then further purifies it by triturating and washing it with hexane. (Jerussi 22: 25-26.)

Given Jerussi's teachings, one skilled in the art would have known pure venlafaxine was *colorless* and would have been motivated to purify the "pale yellow solid" (not a "gum" as Appellants contend, because the gum is described as becoming a pale yellow solid) in order to obtain greater purity. In any case, Appellants claims are not limited to the racemate. Thus, Jerussi's teachings regarding 99.95% pure colorless (+)-venlafaxine are just as relevant as those relating to the racemate. Further, the salts of venlafaxine are also colorless (Jerussi 24: 15, 24, 37), confirming pure venlafaxine is not a colored compound.

As previously noted, Appellants do not describe how they determine color or define the term "crystalline" with respect to the claims before us. For that reason, we find the differences between the prior art and the claimed invention are *at most* the color and degree of crystallinity of Jerussi's racemic venlafaxine and Appellants' claimed white crystals.[4]

We acknowledge Appellants' argument that color is not necessarily indicative of a compound's purity and that a compound's color may reflect a polymorphic form of the compound. However, to the extent Appellants suggest a form of venlafaxine is colored, we find otherwise. Based on the evidence of record, we find the skilled artisan would have known substantially pure venlafaxine is colorless. Thus, the skilled artisan would

[4] With respect to Jerussi's (+)-venlafaxine, the only arguable difference is the degree of crystallinity, and, given that it's 99.95% pure and colorless, we find it is more likely than not crystalline.

have been motivated to purify racemic "pale yellow" venlafaxine with a reasonable likelihood of success. The same skilled artisan would also have tried using hexane to do so, given Jerussi's teachings relating to purifying 1-[cyano-(4-methoxyphenyl)methyl]cyclohexanol (see Jerussi, at 22: 15-27), evidencing that hexane is a known extraction solvent. It is error to conclude that "a patent claim cannot be proved obvious merely by showing that the combination of elements was 'obvious to try.' . . . When there is a design need or market pressure to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to anticipated success, it is likely the product [is] not of innovation but of ordinary skill and common sense. In that instance the fact that a combination was obvious to try might show that it was obvious under § 103." K*SR Int'l Co. v. Teleflex Inc.*, 127 S. Ct. 1727, 1742, 82 USPQ2d 1385, 1397 (2007) (internal citations omitted).

Further, Appellants have not claimed solvate or polymorph forms of venlafaxine. Instead, Appellants' claims read generally on any crystalline venlafaxine. Appellants use similar if not the same reagents for purification that Jerussi uses. Jerussi extracts the product with ethyl acetate, Appellants' preferred extractant, and uses hexane to purify a closely related product, obtaining a "colorless solid." (Jerussi, at 22: 27.)

Further, while Jerussi teaches an embodiment where a pale yellow solid of venlafaxine is obtained, the reference also teaches an embodiment where a colorless solid is obtained—one with greater than 99.95% purity (Jerussi 24: 26-32). Thus, with respect to venlafaxine, the skilled artisan would have known the pure compound is colorless, not yellow.

With respect to degree of crystallinity, there is no evidence Jerussi's solids are not crystalline, or at least partially crystalline. Jerussi describes all their compounds as "solids" regardless of the nature of the compound or degree of purity. (*See, e.g.*, (+)-Venlafaxine (>99.95% pure) (Jerussi, at 24); (+)-Venlafaxine-HCl Salt (>99.99% pure) (*id.*).) In any case, the skilled artisan would have reasonably expected to obtain on further purification not only a colorless compound but also a crystalline one.

While Appellants urge that the crystals are preferred over gums and the yellow gum of Jerussi is unstable (Br. 12) this argument ignores the reference's teaching that the gum is converted to a pale yellow solid and also that the optically active, pure isomer is colorless. It also ignores Jerussi's further suggestion of using hexane to purify a product closely related to venlafaxine, again to obtain a colorless solid (Jerussi 22: 25-29).

Appellants further urge that the facts of the present case are similar to those presented in *In re Cofer*, 354 F.2d 664 (CCPA 1966). (Br. 11-12.) However, the facts in *Cofer* differ from those presented. In *Cofer*, the prior art described the compound as a viscous liquid and there was nothing in the prior art to suggest that a crystalline form of the epoxy propane compound would exist. The court held in *Cofer* there was no explanation why it should be found from the references or from common knowledge that a person skilled in the art would regard free flowing crystals to be obvious. *Cofer*, 354 F.2d at 271. In the present case, the examiner has set forth reasons, from the common knowledge of one of ordinary skill in the art (Jerussi) of purification of venlafaxine, why it would have been obvious that purer venlfaxine crystals could readily be obtained.

We agree with the Examiner's position that one of ordinary skill in the pharmaceutical arts would be highly motivated to obtain the purest form of a compound possible when it is used for medicinal purposes. (Answer 9.) Further, one of ordinary skill in the art would have been motivated to use known purification techniques, such as those disclosed in Jerussi and known to those skilled in the art, to obtain purer crystalline forms of venlafaxine. Therefore, when filtered though the knowledge of one skilled in the art of purification of chemical compounds, we find Jerussi would have rendered obvious, if not anticipated, the claimed crystalline venlafaxine compound.

Given the above, the subject matter of claims 1 and 2 would have been obvious to one of ordinary skill in the art at the time of Appellants' invention, absent evidence of unexpected results due to the alleged differences.

Claims 95-98: The Product by Process Claims

Claims 95-98 are product by process claims to a "[w]hite crystalline solid venlafaxine base." The Examiner takes the position the "determination of patentability is based on the product itself" and does not depend on its method of production." (Answer 4 (quoting *In re Thorpe*, 777 F.2d 695, 698 227 USPQ 964, 966 (Fed. Cir. 1985).)

We agree with the Examiner and thus conclude these claims would have been obvious for the reasons given regarding claims 1 and 2, absent some showing of unexpected results.[5]

[5] Further, Jerussi's 99.95% pure, colorless (+)-venlafaxine appears to be of the same or greater purity as Appellants. Thus, an alternative rejection

In any case, the venlafaxine product of claim 95 is obtained by

a) providing a solution of venlafaxine hydrochloride in water,
b) combining the solution of venlafaxine hydrochloride with sodium hydroxide,
c) extracting the combination with an organic solvent to obtain extract,
d) drying the extract,
e) evaporating the extract to obtain a residue,
f) combining the residue with an alkane, and
g) crystallizing venlafaxine base that is a white crystalline solid from the combination of residue and alkane.

Jerussi describes a process of obtaining venlafaxine including steps of:

a) providing venlafaxine in water (Jerussi, at 23: 16-17)

b) combining the solution with sodium hydroxide (Jerussi, at 23: 20-22)

c extracting the combination with ethyl acetate (Jerussi, at 23: 21-23)

d) drying the extract (Jerussi, at 23: 24) and

e) evaporating the residue (Jerussi, at 23: 24).

While Jerussi does not purify his venlafaxine by combining the residue with alkane and crystallizing venlafaxine base that is a white crystalline solid from the combination of residue and alkane, such as hexane, he suggests doing so with his teachings regarding a closely related compound (*see* Jerussi, at 22: 26-28). Further, as the Examiner found, "[c]hoosing an ideal solvent for crystallization and recrystallization is well

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of the claims under 35 U.S.C. § 102 could have been made in view of this compound.

within the purview of an ordinary artisan." (Answer 8.) "A person of ordinary skill is also a person of ordinary creativity, not an automaton." *KSR Int'l Co. v. Teleflex Inc.*, 127 S. Ct. 1727, 1742, 82 USPQ2d 1385, 1397 (2007).

In *In re Best*, 562 F.2d 1252, 1255, 195 USPQ 430, 433-434 (CCPA 1977) (footnote omitted) the court stated:

> Where, as here, the claimed and prior art products are identical or substantially identical, or are produced by identical or substantially identical processes, the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product. . . . Whether the rejection is based on 'inherency' under 35 U.S.C. § 102, on 'prima facie obviousness' under 35 U.S.C. § 103, jointly or alternatively, the burden of proof is the same, and its fairness is evidenced by the PTO's inability to manufacture products or to obtain and compare prior art products.

Given the facts in this case, in order to overcome the Examiner's prima facie case of obviousness, Appellants were required to show their product would not have been obvious in view of Jerussi's teachings by coming forward with evidence of unexpected results. This they have not done. Thus, we agree with the Examiner that claims 95-98 would have been prima facie obvious.

CONCLUSION

The obviousness rejection under § 103(a) of claims 1, 2, and 95-98 over Jerussi is affirmed.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 C.F.R. § 1.136(a) (2006).

AFFIRMED

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KENYON & KENYON LLP
ONE BROADWAY
NEW YORK, NY 10004